mucolipidosis II alpha/beta

Mucolipidosis II alpha/beta (also known as I-cell disease) is a progressively debilitating disorder that affects many parts of the body. Most affected individuals do not survive past early childhood.

At birth, children with mucolipidosis II alpha/beta are small and have weak muscle tone (hypotonia) and a weak cry. Affected individuals grow slowly after birth and usually stop growing during the second year of life. Development is delayed, particularly the development of speech and motor skills such as sitting and standing.

Children with mucolipidosis II alpha/beta typically have several bone abnormalities, many of which are present at birth. Affected individuals may have an abnormally rounded upper back (kyphosis), feet that are abnormally rotated (clubfeet), dislocated hips, unusually shaped long bones, and short hands and fingers. People with this condition also have joint deformities (contractures) that significantly affect mobility. Most children with mucolipidosis II alpha/beta do not develop the ability to walk independently. Affected individuals have dysostosis multiplex, which refers to multiple skeletal abnormalities seen on x-ray.

Other features of mucolipidosis II alpha/beta include a soft out-pouching around the belly-button (umbilical hernia) or lower abdomen (inguinal hernia), heart valve abnormalities, distinctive-looking facial features that are described as "coarse," and overgrowth of the gums (gingival hypertrophy). Vocal cords can stiffen, resulting in a hoarse voice. The airway is narrow, which can contribute to prolonged or recurrent respiratory infections. Affected individuals may also have recurrent ear infections, which can lead to hearing loss.

Frequency

Mucolipidosis II alpha/beta is a rare disorder, although its exact prevalence is unknown. It is estimated to occur in about 1 in 100,000 to 400,000 individuals worldwide.

Genetic Changes

Mutations in the *GNPTAB* gene cause mucolipidosis II alpha/beta. This gene provides instructions for making part of an enzyme called GlcNAc-1-phosphotransferase. This enzyme helps prepare certain newly made enzymes for transport to lysosomes. Lysosomes are compartments within the cell that use digestive enzymes to break down large molecules into smaller ones that can be reused by cells. GlcNAc-1-phosphotransferase is involved in the process of attaching a molecule called mannose-6-phosphate (M6P) to specific digestive enzymes. Just as luggage is tagged at the airport to direct it to the correct destination, enzymes are often "tagged" after

they are made so they get to where they are needed in the cell. M6P acts as a tag that indicates a digestive enzyme should be transported to the lysosome.

Mutations in the *GNPTAB* gene that cause mucolipidosis II alpha/beta prevent the production of any functional GlcNAc-1-phosphotransferase. Without this enzyme, digestive enzymes cannot be tagged with M6P and transported to lysosomes. Instead, they end up outside the cell and have increased digestive activity. The lack of digestive enzymes within lysosomes causes large molecules to accumulate there. Conditions that cause molecules to build up inside lysosomes, including mucolipidosis II alpha/beta, are called lysosomal storage disorders. The signs and symptoms of mucolipidosis II alpha/beta are most likely caused by the lack of digestive enzymes within lysosomes and the effects these enzymes have outside the cell.

Mutations in the *GNPTAB* gene can also cause a similar but milder disorder called mucolipidosis III alpha/beta. Instead of preventing the production of any enzyme, these mutations reduce the activity of GlcNAc-1-phosphotransferase. Mucolipidosis III alpha/beta and mucolipidosis II alpha/beta represent two ends of a spectrum of disease severity.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- I-cell disease
- inclusion cell disease
- MLII
- mucolipidosis II
- mucolipidosis type II

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: I cell disease
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C2673377/

Other Diagnosis and Management Resources

- GeneReview: Mucolipidosis II
  https://www.ncbi.nlm.nih.gov/books/NBK1828
- MedlinePlus Encyclopedia: Clubfoot
  https://medlineplus.gov/ency/article/001228.htm
- MedlinePlus Encyclopedia: Contracture deformity
  https://medlineplus.gov/ency/article/003185.htm
- MedlinePlus Encyclopedia: Kyphosis
  https://medlineplus.gov/ency/article/001240.htm

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Clubfoot
  https://medlineplus.gov/ency/article/001228.htm
- Encyclopedia: Contracture deformity
  https://medlineplus.gov/ency/article/003185.htm
- Encyclopedia: Kyphosis
  https://medlineplus.gov/ency/article/001240.htm
- Health Topic: Metabolic Disorders
  https://medlineplus.gov/metabolicdisorders.html

Genetic and Rare Diseases Information Center

- I cell disease
  https://rarediseases.info.nih.gov/diseases/6749/i-cell-disease

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Mucolipidoses Fact Sheet
  https://www.ninds.nih.gov/Disorders/All-Disorders/Mucolipidoses-Information-Page

Educational Resources

- Disease InfoSearch: Mucolipidosis II
  http://www.diseaseinfosearch.org/Mucolipidosis+II/3706
- MalaCards: mucolipidosis ii alpha/beta
  http://www.malacards.org/card/mucolipidosis_ii_alpha_beta
- Orphanet: Mucolipidosis type II
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=576

Patient Support and Advocacy Resources

- ISMRD: The International Advocate for Glycoprotein Storage Diseases
  http://www.ismrd.org/
- Lysosomal Diseases New Zealand
  http://www.ldnz.org.nz
- National MPS Society
  http://mpssociety.org/mps/ml-ii-ml-iii/
- National Organization for Rare Disorders (NORD): I Cell Disease
  https://rarediseases.org/rare-diseases/i-cell-disease/
- The Canadian Society for Mucopolysaccharide & Related Diseases Inc.
  http://www.mpssociety.ca
- The MPS Society (UK)
  http://www.mpssociety.org.uk/diseases/related-diseases/ml-ii/

GeneReviews

- Mucolipidosis II
  https://www.ncbi.nlm.nih.gov/books/NBK1828

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22mucolipidosis+type+II%22+OR+%22Mucolipidosis+Type+II%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28mucolipidosis+type+ii%5BTIAB%5D%29+OR+%28i-cell+disease%5BTIAB%5D%29+OR+%28inclusion+cell+disease%5BTIAB%5D%29+OR+%28mucolipidosis+ii%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- MUCOLIPIDOSIS II ALPHA/BETA
  http://omim.org/entry/252500

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